America's Blood Centers

OUR MEMBERS SERVE COMMUNITIES NATIONWIDE

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket #99D-5347: Guidance for Industry: Precautionary Measures to Reduce the Possible Risk of Transmission of Zoonoses by Blood and Blood Products from Xenotransplantation Product Recipients and Their Contacts.

Dear Dockets Management Staff:

America's Blood Centers (ABC) is pleased to comment on the Center for Biologics Evaluation and Research's draft guidance setting out precautionary measures to reduce the possible risk of transmission of zoonoses by blood and blood products from xenotransplantation recipients and their contacts. For your information, ABC is a consortium of not-for-profit, community blood centers that collect about half of the US supply from volunteer blood donors.

In summary:

- ABC members agree with CBER that blood donated by recipients of live cell xenotransplants may pose a theoretical risk to transfusion recipients because of the potential for transmission of known or as-yet unknown infectious agents. Thus, ABC agrees that these xenotransplant recipients should not donate blood or tissues.

- However, ABC does not agree with the deferral of contacts of xenotransplant recipients. There are millions of individuals who have been in contact with animal tissues without evidence of retroviral infection.

- ABC members also believe that the approach taken in the draft guidance—requiring three new questions in the medical history form—is inappropriate and actually may increase the risk of transmission of *known* infectious diseases to blood recipients. Given the complexity of the medical history form, any additional questions risk diverting the attention of donors from those related to major risks to the blood supply (*e.g.* donors in the window of seroconversion for hepatitis and HIV). Instead, ABC believes that the primary responsibility for educating xenotransplant recipients about not donating blood should lie with the medical institutions performing the clinical trials. In fact, at its meeting last month, the Xenotransplant Subcommittee of the Biological Response Modifiers Advisory Committee endorsed this approach at its January 13, 2000 meeting.

- In addition, ABC strongly recommends that before mandating any new additions to the donor medical history FDA must require scientific documentation that the additions will not decrease the safety of the blood supply for known infectious agents such as HIV, HCV, HBV.

Additional history questions affect a large number of donors. Volunteer blood donors donate over 13,000,000 units of whole blood and apheresis platelets every year; the plasma industry collects double this number of units of plasma by plasmapheresis every year. Moreover, at each donation, these donors are screened with an ever-increasing number of questions required by FDA and the American Association of Blood Banks.

The current medical history questionnaires are extensive. The Uniform Donor Questionnaire of the American Association of Blood Banks (*Association Bulletin* #99-10, December 2, 1999) has 32 separate questions. Many of these questions are complex and refer donors to unusual entities and issues: *e.g.*, babesiosis, Chagas, Creutzfeldt-Jakob disease, bovine-derived insulin, human-derived pituitary growth hormone, Acitretin, Proscar, dura mater, Isle of Man, Channel Islands, Immunoglobulin, clotting factor concentrates, etc.

Other history questions address risk behavior, but focus donors' attention on events that took place a long time ago, despite evidence that the major risks of transmission of infectious disease are associated with window periods of weeks, *e.g.* "Have you had sex with another man since 1977?"

In an anonymous post-donation survey carried out in the context of the NHLBI-funded Retrovirus Epidemiology in Donors Study (REDS), 1.9% of donors revealed information that would have led to their deferral as blood donors at the time of donation. (Williams et al, JAMA 277:967-972, 1997)

Xenotransplants are relatively rare events. FDA had declared that clinical protocols proposing their use should not be submitted until further safety data becomes available; thus xenotransplants cannot be performed even under research protocols.

Recipients of xenotransplants are known to the program that sponsored the transplant. ABC members believe that the responsibility for the safety of xenotransplants should be assigned to the people and institutions performing these experiments. We interpret the fact that FDA has not allowed these experiments to continue as *de facto* recognition of these risks and responsibilities. ABC members also believe that institutions performing xenotransplants are equipped with specific means to notify individuals at risk and require that they abstain from donating blood and tissues. This certainly will be more effective than searching for xenotransplant recipients among millions of individuals who show up to donate blood.

ABC's alternative proposal. Blood collecting facilities would include in the written information provided to donors a definition of xenotransplants and an explanation why these recipients should not donate blood or tissues. FDA should require that every past xenotransplant recipient be notified that they are indefinitely deferred from donating blood or tissues. These individuals should be made aware of the theoretical adverse consequences associated with the transfusion of their blood or transplantation of their tissues to another recipient.

Deferring Contacts. The requirement in the draft guidance that blood centers defer as donors "sexual partner(s), any member of your household, or any other close contact" is ambiguous and unsupported by any evidence that a xenotransplant recipient has transmitted a pathogen to a contact. Deferral of "health care workers, laboratory personnel, and other individuals who have had contact with blood and body

fluids from a xenotransplantation product recipient, through percutaneous inoculation (such as accidental needlestick) or through contact with an open wound, non-intact skin, or mucous membranes" is subject to the same criticism. We agree with the proposal made by the AABB to the Xenotransplant Subcommittee that a risk assessment be undertaken among those with close contact to the relevant species for evidence of transfusable disease associations that would support zoonotic transmission of disease-causing organisms.

Additional Concerns about the Blood Donor Medical History Process. On a more general issue, ABC has further concerns about the blood donor medical history. ABC members are extremely concerned about the lack of information about the sensitivity, specificity and predictive value of donor questions. There are no data showing the impact of additional complex questions in the safety (sensitivity) or availability (specificity) of the blood supply. Moreover, there has been no quantitative assessment of the benefit of such additional questions (positive predictive value)

ABC believes that before mandating any new additions to the donor medical history FDA must require scientific documentation that the additions will not decrease the safety of the blood supply for known infectious agents such as HIV, HCV, HBV.

Thank you for the opportunity to comment.

Yours truly,

Celso Bianco, M.D.
President
America's Blood Centers